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## Hematological and immunological profile of ART-Naïve HIV-infected patients in Bali-Indonesia: a descriptive study

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**Abstract.** HIV infection often comes with hematological and immunological profile abnormalities. These abnormalities may occurred because of HIV infection itself or other factors. Therefore we conducted this study to assess the hematological and immunological profile among ART-naïve HIV-infected patients in Bali. This is a descriptive cross-sectional study using data extracted from medical records of HIV-infected patients at Wangaya Hospital Denpasar-Bali and Sanjiwani Hospital Gianyar-Bali. A total of 169 medical records of HIV infected patients between 2009 -2017 were included in this study. Hematological parameters (total WBC, RBC, Hgb, MCV, MCH, MCHC, and Plt) and immunological parameter (CD4+ cell count) were documented. Most of the subjects in this study were male (65.1%) and predominantly (71%) in highly reproductive age group (18-40 years). Anemia (Hb<13.0 g/dL for men or Hb<12.0 g/dL for women) was the most common (60.4%) haematological abnormalities seen in this study and 67.4% in severe immunodeficiency condition (CD4 cell count <200 cells/mm<sup>3</sup>). Statistical analyses performed and the result shows there was an association between anemia and immunodeficiency status ( $p<0.05$ , Pearson Chi-square).

### 1. Introduction

Human immunodeficiency virus (HIV) infection remains a global health problem in most of countries in the world. At the end of the year 2015, there was as much as 2.1 million new infections from total number 36.7 million of infected individuals worldwide [1,2]. It's not only give a huge impact on individual health and health system but also have an impact on country's socioeconomic conditions. In Indonesia, it is estimated 735,256 people living with HIV/AIDS with the number of new infections as many as 85,523 people. The case fatality rate (CFR) due to HIV/AIDS by the year 2015 in Indonesia amounted to 0.95% [3]. In Bali, the number of HIV/AIDS cases tend to be increasing every year. Up to December 2015, the number of HIV infection cases and AIDS cases in Bali reached 1,563 cases and 966 cases respectively [4]. The using of antiretroviral in HIV infection has been dramatically increase the life-expectancy of the patients. Since the number of older people living with HIV infection expands, the new importance problems of ageing-related co-morbidities such as osteoporosis, dyslipidemia has increased [5,6].

HIV infection manifests in a variety of symptoms and also often comes with complications. Hematologic abnormalities are commonly reported among HIV-infected patients, either caused by HIV infection itself or caused by the side effects of the antiretroviral drugs taken by the patient. Hematological abnormalities that commonly occur are anemia, leukopenia, neutropenia, and



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thrombocytopenia and lymphopenia. A study conducted by Akinbami et al. report that there are about 20% of patients undergoing hematologic profile abnormalities before the antiretroviral therapy (ART) is given (ART-naïve patients) [7]. The other study conducted by Leroi et al. report the incidence of neutropenia and anemia are 15% and 31% respectively in patients who get antiretroviral therapy for HIV [8]. Similar results were also reported by Parkes-Ratanshi et al. that get incidence of anemia by 15% in patients who have been getting antiretroviral therapy [9]. Another study conducted in Indonesia reported the incidence of anemia in ART-naïve HIV-infected patients in Java's population amounted to 49.6% [10]. Some studies revealed that hematologic abnormalities, especially anemia, relates to the severity of the disease [11,12]. This study aims to assess the hematologic and immunologic profile of ART-naïve HIV-infected patients in Bali-Indonesia. Study was conducted in Wangaya Hospital Denpasar-Bali and Sanjiwani Hospital Gianyar-Bali.

## 2. Material and methods

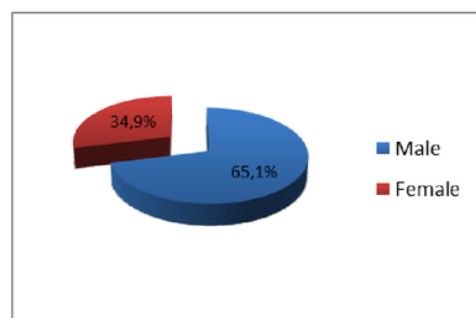
A cross-sectional study was conducted from June to October 2017 in Wangaya Hospital, a referral hospital for Denpasar and surrounding areas, and in Sanjiwani Hospital, referral hospital for eastern area of Bali. Data are obtained from 169 medical records of adult ART-naïve HIV infected patients between 2009-2017. Demographic data (age and sex), hematological profile (total WBC, RBC, Hb, MCV, MCH, MCHC, and Plt) and immunological profile (CD4+ cell count) were documented. WHO/ACTG criteria were used to define mild (Hb 10.5-12.99 g/dL for men; Hb 10.5-11.99 g/dL for women), moderate (Hb 8.0-10.49 g/dL) and severe (Hb < 8.0 g/dL) anemia [13]. Immune status was defined as severe immune deficiency (CD4 count < 200 cells/mm<sup>3</sup>), mild-advanced immune deficiency (CD4 count 200-499 cells/mm<sup>3</sup>) and no significant immune deficiency ( $\geq$  500 cells/mm<sup>3</sup>) [14].

The study was approved by Medical Faculty of Udayana University/Sanglah Hospital Research and Ethics Committee (Approval No. 2043/UN 8 4.2/KEP/2017). Characteristic of patients are presented as number (%), means ( $\pm$  standard deviation) or median (interquartile range). Frequencies and percentages were calculated for all the categorical variables. Pearson Chi-square test was used to determine significant trends in the percentage of patients with a given grade of anemia at different level of CD4 cell count. p value <0.05 was considered statistically significant.

## 3. Result and discussion

### 3.1. General characteristics of the patients

The age of patients in this study were in the range of 18-82 years old with median of 34 years old. Most of the subject (65.1%) are male and one third of the subjects are female (34.9%) (Figure 1). Patients predominantly in the age group <40 years old (71%) and the rest were in the age group >40 years old (29%).



**Figure 1.** Characteristic of patients based on sex.

This result consistent with a pattern characteristic of the age and sex recorded in the data center and information (Ministry of Health) in Indonesia. HIV/AIDS cases have been reported since 1987 until 2014, most cases on the age group 20-39 years [15]. This group is the highly reproductive age group and at high risk for getting HIV/AIDS infection. The pattern of HIV infection transmission on the basis of sex also follows the same pattern in the last few years, infection predominantly occurred in men compared to women's groups.

### 3.2. Hematological profile

Complete blood count data obtained including white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelets (Plt). The mean RBC, Hgb and Hct were  $4.3 \pm 0.6 \times 10^6 / \mu\text{L}$ ,  $12.2 \pm 1.9 \text{ g/dL}$  and  $36.4 \pm 5.37\%$  respectively, while the median of WBC, MCV, MCH, MCHC and Plt were  $5.6 (2.9) \times 10^3 / \mu\text{L}$ ,  $86.0 (7.6) \text{ L}$ ,  $28.6 (2.8) \text{ pg/cell}$ ,  $33.6 (2.1) \%$  and  $236.0 (102.5) \times 10^3 / \mu\text{L}$  respectively (table 1).

Further analysis of our data revealed that of 169 patients in this study, 102 (60.4%) had anemia, out of which 77 (45.6%) had mild anemia, 21 (12.4%) had moderate anemia and only 4 (2.4%) patients had severe anemia (Table 2).

**Table 1.** Baseline hematological profile of the patients.

Hematological profile	Value (n=169)
WBC ( $\times 10^3 / \mu\text{L}$ ), median (IQR)	5.6 (2.9)
RBC ( $\times 10^6 / \mu\text{L}$ ), mean ( $\pm$ SD)	$4.3 \pm 0.6$
Hgb (g/dL), mean ( $\pm$ SD)	$12.2 \pm 1.9$
Hct (%), mean ( $\pm$ SD)	$36.4 \pm 5.37$
MCV (L), median (IQR)	86.0 (7.6)
MCH (pg/cell), median (IQR)	28.6 (2.8)
MCHC (%), median (IQR)	33.6 (2.1)
Plt ( $\times 10^3 / \mu\text{L}$ ), median (IQR)	236.0 (102.5)

**Table 2.** Degree of anemia based on WHO classification system.

Hb concentration (g/dL)	Group	Number (%) N=169
$\geq 13.0$ (men) or $\geq 12.0$ (women)	No anemia	67 (39.6)
10.5 – 12.99 (men) or 10.5 – 11.99 (women)	Mild anemia	77 (45.6)
8-10.49	Moderate anemia	21 (12.4)
< 8	Severe anemia	4 (2.4)

This study highlights a high (60.4%) prevalence of anemia among ART-naïve HIV-infected patients. According to the WHO definition, anemia defined as Hb concentration  $< 12 \text{ g/dL}$  for females and  $< 13 \text{ g/dL}$  for males. This result is quite high comparing with another studies in Java's population and in Kathmandu, Nepal [10,11]. It may because of most HIV-infected patients in Bali do not seek medical attention until they come in the advanced stage.



There are many hypotheses in the mechanism of anemia among HIV-infected patients. The infection that caused by a chronic illness can disrupt cytokines homeostasis in bone marrow. Infection by HIV virus is cytotoxic against T-helper lymphocytes which resulted in deregulation of B-cells and changes in cytokines homeostasis. T-cells that are infected with HIV virus can directly suppress the growth of progenitor cells in the bone marrow so that affecting the hemopoiesis [16].

### 3.3. Immunological profile

Of 169 patients in this study, only 141 patients had CD4 cell count data available with median CD4 cell count was 87.0 (220.0) cells/mm<sup>3</sup>. Based on CD4 cell count, immunodeficiency status of the patients can be classified into no significant immunodeficiency (1.4%), mild-advanced immunodeficiency (31.2%) and severe immunodeficiency (67.4%) (Table 3).

**Table 3.** Immunodeficiency status based on CD4 cell count.

CD4 cell count (cells/mm <sup>3</sup> )	Group	Number (%) N=141
≥500 cells/mm <sup>3</sup>	No significant immunodeficiency	2 (1.4)
200-499 cells/mm <sup>3</sup>	Mild-advanced immunodeficiency	44 (31.2)
<200 cells/mm <sup>3</sup>	Severe immunodeficiency	95 (67.4)

CD4 cell count can be used to measure the degree of immunosuppression in HIV-infected patients. Several studies have shown that CD4 cell count is a predictor of disease progression and survival. Low initial CD4 cell count is predictive of rapid progression of untreated HIV-1 infection [17]. Patients starting antiretroviral therapy with CD4 cell count >200 cells/mm<sup>3</sup> show low rates of disease progression to AIDS and death [18].

Furthermore, the immunodeficiency status was classified into immunodeficiency (severe immunodeficiency) and no immunodeficiency (no and mild-advanced immunodeficiency). Out of 141 patients, 64 (45.4%) had anemia and in immunodeficiency condition, 31 (22.0%) had no anemia but in immunodeficiency condition, 21 (14.9%) had anemia but had no immunodeficiency status and 25 (17.7%) neither had anemia and immunodeficiency status. Further analyses indicate an association between anemia status and immunodeficiency status ( $p < 0.05$ , Chi-square test) (Table 4).

**Table 4.** Severity of immunodeficiency based on anemia status.

Anemia	Immunodeficiency		P-value
	Yes	No	
Yes	64	21	0.013*
No	31	25	

\*Pearson Chi-square test

Further analysis of our data revealed an association between anemia and immunodeficiency status ( $p < 0.05$ , Chi-square test). Prevalence of anemia, leukopenia, thrombocytopenia and lymphopenia are increased as the decrease in the CD4 cell count. The severity of hematologic abnormalities is increased along with the decrease in CD4 and have a significant impact disease outcome and quality of life of the patients. It is therefore important to identify the hematologic abnormalities in patients with HIV so that morbidity and mortality can be minimized [19,20]. Besides, early detection of HIV is one of the important strategies to reduce complications of hematologic abnormalities and severity of

immunodeficiency due to HIV infection. In addition with early detection then ART therapy can begin immediately so can improve the disease outcome.

#### 4. Conclusion

The prevalence of anemia and immunodeficiency in ART-naive HIV-infected patients in Bali is high. The analyses result indicates association between anemia and immunodeficiency status. Early detection is important as ART can begin immediately so can improve the disease outcome.

#### 8 Acknowledge

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